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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/799,005	03/11/2004	James Rasmussen	PEPT-P01-005	7191

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EXAMINER	
SZPERKA, MICHAEL EDWARD	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 11/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/799,005	RASMUSSEN ET AL.	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-11 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-11 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 06/23/04.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-11 are pending and under examination in the instant application.

It is noted that Applicant indicates the disease pemphigus vulgaris as *Pemphigus vulgaris*. The disease is not a microorganism, and as it seems unlikely that Applicant wishes to emphasis the name of the disease at every occurrence, the name should not be italicized. However, the phrase *in vitro* found on page 1 in the section titled Field of the Invention, should be italicized. Additionally, a review of pemphigus vulgaris (PV) literature indicates that pemphigus is normally only capitalized if it is the first word of a sentence. Appropriate correction is suggested.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Oath/Declaration

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant has claimed a polypeptide and composition that consists essentially of SEQ ID NO: 1, a 19 amino acid fragment of the cellular adhesion molecule desmoglein 3. The phrase consisting essentially of is defined by applicant on page 19 of the specification as encompassing the addition of no more than 30 amino acids or peptidomimetics to a sequence consisting of SEQ ID NO: 1. This definition also indicates that the added sequence does not substantially alter the function of the designated sequence, although the meaning of substantially is unclear. The disclosure does not appear to give guidance in selecting the length of the desmoglein 3 polypeptide to be used in the invention, as the discussion of self and foreign epitope selection that begins on page 50 indicates that such peptides are 15 amino acids long, yet SEQ ID NO: 1 is 19 amino acids long. Applicant indicates on page 51 that longer peptides are contemplated, but the length of such peptides is not specified. In particular, guidance appears to be lacking as to why the addition of 4 amino acids from

the native sequence of desmoglein 3 to the 15 amino acid sequence disclosed as SEQ ID NO: 3 in U.S. Patent No. 5,874,531 is an improvement over the prior art, as this reference also indicates that longer peptides are considered as equivalents.

The peptide and composition claimed by Applicant can be used to treat patients with PV or to create animal models of PV as disclosed on page 52 of the specification. There does not appear to be any difference in how the peptide is administered that would lead to the selective induction of tolerance or a breaking of tolerance in a patient, human or otherwise. As such, it is puzzling that the same composition can have such dramatically different utilities based on the instant disclosure.

The efficacy of treating PV by administering a single peptide of desmoglein 3 is uncertain. Veldman et al. recently discovered that autoreactive T cells specific for a desmoglein 3 epitope that corresponds to SEQ ID NO: 1 can be found in PV patients and healthy controls (J. of Immunol., 2004, 172:3883-3892, see entire document, particularly Figure 2 and the last paragraph of the discussion). These findings clearly demonstrate that T cell recognition of epitopes from desmoglein 3, including epitopes that correspond to SEQ ID NO: 1, is independent from the development of pemphigus vulgaris (see particularly the last sentence of the abstract). Also, the phenomenon of epitope spreading occurs in many autoimmune diseases, PV included. Intramolecular epitope spreading has not been reported (see particularly Veldman et al., page 3890, first full paragraph of the right column), but intermolecular spreading to other antigens, notably desmoglein 1, has been reported in patients that develop cutaneous forms of PV (see Veldman et al., page 3890, last sentence of the first full paragraph of the right

column, and Goon et al., Clinical and Experimental Dermatology, 2001, 26:661-663, see entire document, particularly page 662, the first full paragraph). This phenomenon makes the use of peptide-specific treatment for chronic autoimmune diseases impractical, as the initiating epitope and the pattern by which other epitopes become involved is unpredictable and can vary from individual to individual, as discussed by Vanderlugt and Miller (Nature Reviews Immunology, 2002, 2:85-95, see particularly page 92, the section titled Treatment of autoimmunity and transplant rejection). As such, the use of peptide-specific treatments for human diseases is currently difficult (see particularly Vanderlugt, page 92, last sentence of the third full paragraph of the left column). The variability of the initiating epitope(s) in PV is documented by Veldman et al. in Table I, page 3885, and it is noteworthy that autoreactive T cells specific for the epitope corresponding to SEQ ID NO: 1 were only seen in 2 of 16 patients.

Therefore, it appears that an undue amount of experimentation would be left to a person of skill in the art to use Applicant's claimed invention based on the lack of working examples, the lack of guidance concerning the use of the same composition to induce tolerance and induce autoimmunity, and the unpredictability of using peptide-specific compositions to treat diseases in humans. In particular, given the occurrence of autoreactive T cells specific for SEQ ID NO: 1 in healthy controls, it is not at all clear how or if the epitope of SEQ ID NO: 1 is linked to the development and treatment of PV.

5. Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicant has claimed a polypeptide and composition that consists essentially of SEQ ID NO: 1, a 19 amino acid fragment of the cellular adhesion molecule desmoglein 3. The phrase consisting essentially of is defined by applicant on page 19 of the specification as encompassing the addition of no more than 30 amino acids or peptidomimetics to a sequence consisting of SEQ ID NO: 1. This definition also indicates that the added sequence does not substantially alter the function of the designated sequence, although the meaning of substantially is unclear. Peptidomimetics, and the range of molecules contemplated as being peptidomimetics are disclosed in the paragraph that spans pages 22 and 23 and the third full paragraph of page 34. Some functional attributes ascribed to peptidomimetics include non-hydrolyzability, increased specificity and increased potency (see page 30, first full paragraph). Some examples are provided on pages 28-34, but it is still unclear as to what the structures of the peptidomimetics will be given the great variability in the kinds of molecules identified as peptidomimetics. The list on page 34 includes protein-based, carbohydrate-based, lipid-based, nucleic acid-based, natural organic, and synthetic organic compounds, as well as anti-idiotypic antibodies, catalytic antibodies and fragments of antibodies.

As indicated above, the only requirement of peptidomimetics is that they be functional. The particular function that must be maintained does not appear to be

specified, and the items listed as potential peptidomimetics are not united by any common structure. As such, variation in the structural and functional properties of such a genus of molecules as are encompassed by the broadest reasonable interpretation of the claims is substantial.

Thus, Applicant has claimed the broad genus of peptidomimetics and longer peptides when only the species of SEQ ID NO: 1 is disclosed. The structure and function of peptidomimetics and longer peptides consisting essentially of SEQ ID NO: 1 has not been disclosed, nor has a relationship between the structure of the peptidomimetics or longer peptides and the resulting function been established. MPEP section 2163.05 clearly states that when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

As indicated above, there is substantial variation within the claimed genus peptidomimetics and longer peptides that consist essentially of SEQ ID NO: 1. Since there is high variability amongst the genus of molecules of the claimed invention, and Applicant has disclosed only SEQ ID NO: 1, the claimed invention does not have written support within the originally filed specification. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, which make clear that if a claimed genus does not show actual reduction to practice for a representative number of species, then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional

characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus.

6. No claims are allowable.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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October 25, 2004

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